2.1 THERMOSENSITIVE HYDROGEL

ISGS of Moxifloxacin HCl were developed. The developed formulations increases the residing time of the drug at the site and found to be promising in all respect Nanjwade B et al (2012) [60].

The applicability of IS thermo sensitive hydrogel containing chitosan along with α-d-Glucose one-PO4 disodium was evaluated and found that the chitosan and DGP thermosensitive IS gel can be tolerated well Chen X et al (2012) [61].

A thermo reversible IS gel of Moxifloxacin HCl using bioadhesive polymer was prepared. Drug polymer interaction study whatever performed revealed no interaction. In vitro release tests proved that the IS gel provides prolonged retention time Dholakia M et al (2012) [62].

Thermo sensitive diclofenac sodium ophthalmic IS gels has optimized and evaluated. Increase of PXM 407 content decreased transition temperature of the products. CP 940 did not show any effect on transition temperature, since transparency, pH and capacity to gel get affected Asasutjarit R et al (2011) [63].

IS gelling nano-emulsion form of dorzolamide was formulated. Evaluation of the system showed better in vivo performance, fast action of onset and long effect compared with that of either drug solution or the marketed product Ammar H et al (2010) [64].

Effect of salts on methylcellulose based IS gels were studied. It was found that certain salts decreases gel temperature below physiological conditions Bhowmik M et al (2010) [65].
An ophthalmic carrier system of the forskolin was developed, based on IS gelation using PXM 407 **Gupta S et al** (2010) [66].

ISGS for delivery of azithromycin was developed. Addition of CP 974P to the ISGS increases solubility due to salting and enhance the bioadhesive capacity of the system **Cao F et al** (2010) [67].

ISGS of Moxifloxacin HCl was formulated. Two PXM systems viz. PXM 407/ PXM 188 were used. Different viscosity building polymers were used such as XG and sodium alginate with view to increase gelling and bioadhesive capacity **Shastri D et al** (2010) [68].

An ocular gel formulation of fluconazole was developed. Thermo reversible gels were prepared with PXM 407 and different muco-adhesive polymers. The formulated gels were transparent, homogenous and show good covering properties with acceptable pH values **Gonjari I et al** (2009) [69].

The effect of HA on the gelation of PXM was studied. Micellar diameter of PXM was evaluated by PCS **Mayol L et al** (2008) [70].

CFX Hcl ISGS using PXM 407 and PXM 188 was prepared. IS forming gel formulae showed optimum release, bioadhesion properties and improved eye bio-availability evaluated comparatively with eye drops **Mansour M et al** (2008) [71].

Similarly, **Ma W et al** (2008) demonstrated on his findings that pluronic-g-PAA copolymer may measurably increases the drug residing time and pharmacological activity [72]; **Ma W et al** (2008) showed that drug resident time and concentration in conjunctival sac of rabbit has increased considerably for F127-g-poly copolymers as
ISG system evaluated comparatively with conventional formulations [73]; Hongyi Qi et al (2007) developed ISG systems of puerarin based on PXM analogs and CP [74];

Dumortier G et al (2006) the effect of cysteine on PXM was evaluated and concluded that cysteine addition produced only slight but considerable decrease in gelling temperature and show more gel strength [75]; Yoo M et al (2005) studied CPX release behavior in vitro, adhesion and morphology of human lens cells using graft copolymer [76]; Cho K et al (2003) developed gel and liposome based formulations of CPX to minimize tear-facilitating dilution in the conjunctival sac [77];

Jeong B et al (2002) summarized the thermosensitive polymeric systems with focus on the responsible transition ways and potential delivery aspects [78]; Ricci E et al (2002) prepare gels with different concentrations of PXM 407 and additives e.g. inorganic salts and PEG 400 which can change the releasing process of lidocaine [79]; Kim E et al (2002) prepared rhEGF/PXM gel to study its suitability for ophthalmic delivery [80]; Miyazaki S et al (2001) evaluated thermoreversible gel of an enzyme-degraded xyloglucan poly-saccharide for the delivery of pilocarpine hydrochloride [81]; Lin H et al (2000) proved that the CP and pluronic combination could be used as an IS gelling carrier to enhance the bio-availability [82]; Edsman K et al (1998) performed rheological study of PXM system [83]; Pandit N et al (1996) investigated that salts with multivalent anions, at specific concentrations prevents gelling of F127 solutions [84].
2.2 pH SENSITIVE HYDROGEL

Formulation and evaluation of an ISG delivery of Timolol was described. PAA was used in combination with hypromellose. Shelflife determined by Arrhenius equation was found to be 1.6 years Rathor K (2011) [85].

Ocular carrier systems for CPX which undergo sol-to-gel transition were designed. CP and alginites polymers were used with HPMC and MC as viscosity modifier. The release exponents (n), indicating that the drug release took place by zero-order kinetics Al-Kassas R et al (2009) [86].

An ophthalmic carrier for Ketorolac trimethomine and CP 934 was formulated. System was found to be good alternative to conventional formulations. The system showed better bio-availability, longer precorneal residing time. Produce sustained drug release Nanjwade B (2009) [87].

Formulation development t of an ocular carrier system of Ketorolac trimethomine was described. PAA was used together with hydroxy propyl MC. All characteristics of the developed formulations were found to be acceptable Manjappa A et al (2009) [88].

Hydrogels of carbomer and azithromycin were prepared. The hydrogels exhibit pH close to eight and are found physically stable Esteban S et al (2009) [89].

ISGS of CFX hydrochloride was prepared. To get suitability between drug and polymer ion exchange resin were used. The formulation was found to be stable and suitable to eyes as found in rabbits Jain S et al (2008) [90].

Induced bacterial conjunctivitis in rabbit’s eye was treated. The liquid to gel ISGS of CPX showed better improvement when evaluated comparatively with
existing eye drops. Drug concentration in aq. humor was found to be greater than the MIC$_{90}$ with $t_{90}$ of greater than 2 years Charoo V et al (2003) [91].

Similarly, Vilches A et al (2002) prepared hydrogels of model FQ antimicrobials to evaluate their physical and delivery properties [92]; Taberner T et al (2002) studied the polymerization process of PAA, assessing its consistency as a function of the extents of neutralization [93]; sustained ophthalmic delivery of OFX from a pH sensitive ISGS was described. The developed ISG was good in delivery aspects Srividya B et al (2001) [94].
2.3 HYDROGEL CONTAINING CHITOSAN

ISG forming system consisted of PXM/chitosan for enhanced permeation and sustained release of fluconazole was evaluated and found good alternative for IS without chitosan Gratieri T et al (2011) [95].

2.4 LITERATURE ON ION SENSITIVE HYDROGEL

An aesculin-containing ISGS based on deacetylated gellan gum was prepared. PK and eye tissue distribution showed that AG greatly improved aesculin accumulation. The AUC for AG in aq. humor, other parts of the eye were significantly larger than that of aesculin Chen Q et al (2012) [102].

The development of carrier system of brimonidine tartrate was described. The system is based on the theme of ion sensitive IS gelation Geethalakshmi A et al (2012) [103].

IS gel forming ocular drug delivery system of moxifloxacin HCl was prepared. The developed formulations exhibited sustained release over a long period of 10 hr. The formulations were observed as non-irritating, no eye damage or unwanted clinical signs in any part of eyes and increasing residing time of drug Mandal S et al (2012) [104].

Ion activated ISGS, forming gel on eye surface and prolonging corneal contact was studied. The study includes AsODN penetration into the tissue of cornea in the stage of wounding. Significant differences were seen in the delivery efficiency, with the developed systems Rupenthal I et al (2011) [105].

Comparatively gellan, XG, carrageenan, alginate, HPMC and a positively charged chitosan were evaluated. All systems posses good chained polymer networks. Those were able to undisturbed upon apply of shearing and significantly prolonged the in vitro release of hydrophilic drug compared to a reference Rupenthal I et al (2011) [106].

Mol. weight of poly-ethyleneglycol (PEG) and NaCl show effect on the gelation temperature of methylcellulose. The gelation temperature of MC was reduced by 10.4 to 5.9oC with the increasing mol. weight of PEG. It was seen that the drug release
extended from five to eight hours with the ascending order of mol. weight of PEG. This was due to the optimum viscosity and gelling strength Bain M et al (2009) [107].

Timolol in l-carnosine-buffered gellan was comparatively evaluated with Timoptic-XE. Functional synergy with sustained precorneal contact proved as a potential for topical eye dosage forms Singh S et al (2009) [108].

IS gum based ocular drug delivery system of linezolid was prepared. Different viscosity modifiers like HPG, xanthum along with hydroxyethyl cellulose and CP and alginate are used. The formulations observed as non-irritating, no damage or unwanted clinical signs to the various eye parts Hiremath S et al (2008) [109].

Ocular PK of ion activated IS gelling ophthalmic carrier system for gatifloxacin by doing use of microdialysis was studied. The developed formulation was found to have higher bio-availability and longer residing time in aq. humor than conventional Liu Z et al (2007) [110].

A topical ocular gel of atenolol with CMC and sodium alginate in different combinations were formulated. The results revealed that, release rate of drug from gel preparations is inversely proportional to polymer concentration Hassan M et al (2007) [111].

Gellan gum in the preparation of ocular ISG formulation of flurbiprofen sodium was used. The ISG formulation subjected to accelerated stability. In vivo studies confirmed its ISG ability as well as nonirritating and non toxic behavior Kulkarni M et al (2007) [112].
2.5 PHARMACOKINETIC STUDY AND GAMMA SCINTIGRAPHY

Pilocarpine ISG for the eye toxicity, retention time and in vivo release characteristics was evaluated. A study revealed a biphasic rapid release for the solution. A formulation based on different IS gelling systems, observed to deliver at a constant rate Rupenthal I et al (2011) [118].

The relation between the compatibility of baicalin and pH-sensitive ISGS was investigated. CP 974P as gelling agent combined with HPMC E4. In elimination studies, radioactivity of formulation was found to be higher than solution. Additionally, AUC and C\text{max} values were found to be higher Wu H et al (2011) [119].

A PXM/chitosan IS forming gel was formulated. Chitosan improves strength and consistency of formulations. Muco-adhesive properties are proportional to the order of concentration. More than 50% of the gel retained on the corneal surface after ten-min. of instillation, signifies increased retention than a conventional eye drops Gratieri T et al (2010) [120].

A thermosensitive ISG vehicle of methazolamide was prepared. The optimum concentrations of PXM analogs were 21%w/w PXM 407 plus 10%w/w PXM P188. Show in vitro diffusion-controlled release of drug from the ISG vehicle. PXM solutions are good in retaining drug at the eye site Qian Y et al (2010) [121].

Liu Y et al (2010) IS gelling gellan plus an alginate formulation as vehicles for dosing of matrine was studied. The combination of gellan plus alginate solutions showed greater gel strength [122].
Penetration enhancer in combination with gellan gum as gelling agent for timolol was used. The formulation developed has non-irritant nature. Improved drug permeation and prolonged residence was obtained Gupta H et al (2010) [123].

Ocular gels of fourth generation FQ using mucoadhesive polymers were developed. The gels have a required transition and contact Gonjari I et al (2010) [124].
2.6 THE FLUROQUINOLONES

Gupta H et al (2011) developed nanosuspension of FQ drug that retained for the longer time and drained out from the eye very slowly evaluated comparatively to marketed formulation [125];

Bhattaa R et al (2011) studied a new economical and affordable HPLC technique coupled with tandem mass spectrometry (LC-MS/MS) method for ocular PK study of natamycin eye drops in New Zealand rabbit [126];

Heydari A et al (2011) assessed penetration of CFX into the ocular aq. humor. It was concluded that combination of the oral treatment with topical therapy increases aq. humor drug level and also is effective significantly [127];

Similarly, Xuan L et al (2010) compared the drug concentration of gatifloxacin in aq. humor in patients with cataract, administered ISGS with that in patients administered solution of the same strength [128]; Marquar M et al (2010) studied the chemotherapeutic effects and PK properties of a thermosetting ISGS containing 0.3% w/w OFX as well solution [129]; Watanabe R et al (2010) studied the corneal cytotoxicity of two FQ viz. LFX and moxifloxacin eye drops [130]; Sharmap C et al (2008) illustrates the chemistry, pharmacology, PK, antibacterial spectrum and interactions of NFX, which proved vitally important in treatment of several infectious diseases [131];

Hariprasad S et al (2005) investigated the penetration in humans of 0.5% moxifloxacin hydrochloride into the aq. and vitreous after topical administration [132]; Satia M et al (2005) studied the ocular PK of sparfloxacin in the aq. humour of rabbits [133]; Tai M et al (2003) investigated permeability of nalidixic acid and modified FQ and their in vivo PK in model animal as rabbits [134]; Meadows D et al (2002) developed new method which is safe, economical, simple and convenient and
offers comprehensive RT data [135]; Felt O et al (2001) studied ear concentration of tobramycin and OFX after topical application of chitosan-based formulations and evaluated comparatively with 2 existing formulations [136].